DETAILED ACTION

It is noted that the petition to revive this application, filed on 1/8/ 2008, after it was abandoned due to failure to respond was granted on 4/3/2008.

It is noted that the petition to expunge the 8 page document submitted on May 24, 2007, filed on 1/8/ 2008, was granted on 4/15/2008.

Sequence compliance

The application fails to comply with CFR 1.821(d), which states:

> (d)Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

For example, page 14, contains a nucleic acid sequence. Applicant is required to check the rest of the disclosure for any other nucleic acid or protein sequences and list them in a sequence listing and identify them with a proper SEQ ID NO.

The specification and sequence listing must be amended to bring it into sequence compliance. **For any response to this office action to be fully compliant, the response has to bring the application in compliance with sequence rules.**

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 6-10 and 16, in the reply filed on 1/8/2008 is acknowledged. It is noted that the response included species election for claims 6-8, however no species election was required.

2. Claims 1-5, 11-15, and 17-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/8/2008.

3. Applicant's representative agreed that claim 16 properly depends from claim 6. Claim 16 will be treated as it depends from claim 6 per the in discussion with attorney on date 5/1/2008.

Specification

4. The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. An example of an embedded hyperlink is page 13, 3rd line. Applicant is required to inspect the rest of the disclosure and delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

5. The specification is objected to as it presents a figure on page 11. MPEP § 608.01 states, "The specification, including any claims, may contain chemical formulas and mathematical equations, but must not contain drawings or flow diagrams."

Appropriate correction is required.

6. The use of the trademark multiple trademarks including RAPAMUNE™ CERTICAN™, CELLCEPT ™, IMURAN™, NEORAL™ PROGRAFTM have been noted

in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

7. Claims 8-10 are objected to because of the following informalities:

The claims 8 and 10 refer to tables and claim 9 depends from claim 8. MPEP 2173.05(s) states:

Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience."

Claim 16 is objected to as it depends from claim 1, which has been withdrawn. Claim 16 should be amended to depend from claim that is under consideration.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-10 and 16 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The nucleic acid sequences that are critical or

essential to the practice of the invention, but not included in the claims are not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

MPEP 608.01(p)[R-2] states that "While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques, where necessary, as to enable those persons skilled in the art to make and utilize the invention.

Claims 6-10 and 16 are drawn to polynucleotides comprising the nucleic acid sequences on sequence X04500. By referring to the GenBank Accession Number, the claims seek to incorporate by reference the subject matter of the sequences set forth in the recited GenBank records. This constitutes an improper incorporation by reference to essential subject matter since this subject matter is necessary to describe the claimed invention. The contents of GenBank accession numbers can change with sequences being added and deleted which can alter the numbering of nucleotides. Furthermore, reliance upon a SNP identification number which is referenced by a GenBank accession record does not provide adequate clarity for the claimed invention, as the content and numbering in a GenBank record can change over time as the records can be updated as time passes. In this case a potential update to the cited GenBank record wherein a revision includes the addition or deletion would result in a complete change in the numbering system. The reliance of nomenclature of SNP number scheme, which is defined by an external GenBank sequence for a numbering scheme is similar to a recitation of a trademark as the GenBank accession number record does not represent a fixed disclosure of a sequence but instead refers to a record that is constantly able to

be updated and modified. In the instant application, only the nucleic acid sequences of the disclosed SEQ ID No. are described. Also, in Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Essential material may not be incorporated by reference to non-patent publications (see MPEP 608.01(p)). Therefore, the claims are rejected for failure to comply with the enablement requirement because the specification fails to provide essential subject matter for the practice of the claimed invention.

9. Claims 6-10 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining whether a human patient is predisposed to cholesterol of 240 mg/dl in response to treatment with everolimus comprising obtaining a blood sample from patients, isolating genomic DNA from the sample, detecting a C at the -31 position of the IL-1B; detection of a C at position -31 of the IL-1B indicates that the human patient is predisposed to have a cholesterol of 240 mg/dl after 3 years of treatment with everolimus, does not reasonably provide enablement for determining the degrees of serum cholesterol elevation in “any” patient by the detection of “any” mutation in response to treatment with “any” immunosuppressant with “any” length of treatment. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors have been described by the court in re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in the Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

The claim 6 is drawn to a method of determining the degree of serum cholesterol elevation which will occur in a patient during treatment with an immunosuppressant pair at the polymorphic site -31 T>C of IL-1β gene and assigning the patient to the a high cholesterol elevation group if both pairs are CG, assigning the patient to an intermediate elevation group if one pair is AT and one pair is CG and low cholesterol group if both pairs are AT.

Thus claim 6 is broadly drawn to the detection of a mutation of “any” Il-1b gene at a position "any" position that is broadly identified as -31 T>C in “any” patient. The claim is further drawn to classifying based on the presence of GC or AT at position -31.

“Any” patient broadly encompasses dogs, cats, mice, flies, etc, who are on "any" immunosuppressive drugs.

“Any” immunosuppressive drug broadly encompasses cyclosporines, rapamycins, steroids, etc.

IL-1b gene broadly encompasses any IL-1b gene of any species, while the -31 position is any position that can be broadly identified by the recitation.

Claim 7 is drawn to a method of treating “any” patient with immunosuppressive medication by determining the presence of a mutation at position -31 of "any" IL-1b gene and treating the patient with one immunosupressive medication if both pairs are AT and with an alternative treatment if one of more of the alleles is GC.

The recitation of GC, CG, or AT broadly encompasses any dinucleotide with the required sequence.

Claim 8 draws the claim to immunosuppressives listed in Table 2.

Claim 9 draws the claims to immunosuppressive is everolimus.

Claim 10, draws the alternative treatment comprises the addition of a cholesterol lowering medication chosen from those listed in table 1.

Claim 16 is drawn to the methods of determining the identity of the “any” nucleotide pair or haplotype comprises finding “any” SNPs any where in “any” said SNP to determining the nature of the nucleotide pair of interest.

The amount of direction or guidance and the Presence and absence of working examples.

The specification teaches that El-Omar had previously identified the -31 mutation of the Il-1b promoter.

The specification teaches a study of male and female kidney transplant patients that are treated with everolimus (RAD) or mycophenolic acid and mycophenolate Mofetil (MMF) (see figure page 11).

The specification teaches that this study found 47 SNPs in 24 genes that were associated with increased cholesterol in patients treated with RAD (see last paragraph page 11). The specification continues that 21 of the 47 were determined not to be polymorphic (see last paragraph page 11). Two SNPs (-511 and -31) were found to be in the promoter of the Il-1b gene and showed a statistical correlation with increased cholesterol levels (see bottom page 11, to top of page 12). Thus the specification teaches mutations in the promoter of Il-1b were associated with elevated cholesterol in patients treated with RAD. This is not enabling for treatment with “any" immunosuppressive.

The specification continues, “Patients who were homozygous for the IL-1.beta. (-511) C>T base transition (T-T) or the IL-1.beta. (-31) T> C base transition (C-C) had the highest least mean levels of total cholesterol at their last visit regardless of treatment received during the study (p=0.0018 and p=0.0013 respectively). The increase in total cholesterol levels was due to both increased levels of HDL and LDL: patients homozygous for the T allele at the (-511) position or the C allele at the (-31)

position had the highest least square mean levels of HDL (p=0.0214 and p=0.0514 respectively) and LDL (p=0.0159 and p=0.0091 respectively) at their last visit. Importantly, however, the HDL to LDL ratios remained the same regardless of genotype. Therefore, our findings suggest that individuals homozygous for the T allele at position (-511) and homozygous for the C allele at position (-31) of the IL-1.beta. gene promoter may be predisposed to larger increases in total blood cholesterol" (see page 15 1st 3 paragraphs). Thus the specification teaches homozygous C at -31 is indicative of elevated cholesterol. The specification thus teaches patients with immunosuppressive who had the homozygous C at -31 were more likely to have higher cholesterol than those who did not. The specification does not teach the elevation is due to the immunsuppresive treatment, as the specification does not provide data for patients prior to treatment.

The specification in table 5 teaches that patients treated with RAD were statistically elevated regardless of IL-1b genotype (p=0.009), but those treated with MMF were not statistically elevated (p=0.0625). Table 5 further teaches that the effect of the RAD treatment group was great enough to make the combined MMF and RAD groups statistically significant regardless of -31 genotype (p=0.0013). Thus the specification teaches that RAD appears to increase cholesterol regardless of genotype.

The specification in table 7 teaches that patients treated with RAD were statistically elevated HDL regardless of IL-1b genotype (p=0.0205), but those treated with MMF were not statistically elevated (p=0.1893). Table 7 further teaches that the effect of the RAD treatment group on HDL was great enough to make the combined

MMF and RAD groups were not statistically significant regardless of -31 genotype (p=0.0514). Thus the specification teaches that RAD appears to increase HDL, irregardless of genotype.

The specification in table 9 teaches that patients treated with RAD were not statistically elevated HDL regardless of IL-1b genotype (p=0.143), but those treated with MMF were not statistically elevated (p=0.2061). Table 9 further teaches that the the response is sample size dependent, but not genotype dependent as combined analysis of both groups, resulted in p=0.0091, however the individual groups is not statistically associated with increased LDL levels. Thus the specification teaches the IL-1b genotype is not predictably associated with LDL levels.

The specification teaches that CC or CT at the -31 position of the IL-1b promoter was statistically associated with cholesterol being greater than 240 mg/dl (p=0.0096) for treatment with RAD (see table 10).

The specification further teaches that a mutation at -31 disrupts the data box and thus inactivates transcription, thus decreasing transcription (see page 20, 3rd paragraph).

The state of prior art and the predictability or unpredictability of the art:

The Wyllie et al (US PG-PUG 2003/0235890, published December 25, 2003) teaches that the IL-1b -31 polymorphism had no effect on transcriptional regulation of the IL-1b gene (see paragraph 270). Wyllie further teaches, "The previously-unknown -3737 polymorphism lies in a candidate NF-KB binding site in a region of the distal promoter previously shown, by mutagenesis, to be responsible for up to 30% of the

activity of the total promoter. Reproducible and significant differences were found when different alleles of this promoter were placed upstream of a reporter gene. Linkage disequilibrium across this region creates haplotypes with the previously known SNPs at -31 and -511 which were shown in these experiments to have no detectable independent effect on transcription of the reporter gene. The results demonstrate that disease associations with these proximal upstream polymorphisms cannot be explained mechanistically by functional alterations caused by these polymorphisms, themselves, and that their linkage to the newly-discovered function-altering polymorphism at -3737 in the distal upstream promoter is the more likely explanation" (see paragraph 0263). Wylie thus teaches the -31 polymorphism does not alter transcription and thus is not predictably associated with a disease state.

The post-filing art teaches that the presence of the C(-31)T mutation did not result in altered cholesterol synthesis in polish children (see Pediatia Polska (2004) volume 79, pages 127-134).

Brenner et al (Trends in Genetics (2001) volume 17, pages 414-418) teaches that, "Here, the 'homology-implies-equivalency' assumption is restricted to a subset of homologs that diverged in the most-recent common ancestor of the species sharing the homologs. This strategy is useful, of course. But it is likely to be far less general than is widely thought. Two species living in the same space, almost by axiom, cannot have identical strategies for survival. This, in turn, implies that two orthologous proteins might not contribute to fitness in exactly the same way in two species" (see page 414, 3rd column last full paragraph). Brenner specifically describes that although the leptin gene

homologs have been found in mice and humans, their affect is different (see page 414, 3rd column last paragraph-3rd column page 415). Brenner specifically teaches that the leptin gene in mice plays a major role in obesity, but no such effect has been demonstrated in humans due perhaps to the different evolutionary forces. Brenner thus teaches that the activity and function of genes in different species is unpredictable.

Moore et al teaches that treatment with immunosuppressants is commonly associated with persistent increases in total cholesterol (Drug Safety (2001) volume 24, pages 755-766)(see abstract). Moore et al teaches that immunosuppressants most commonly associated with increased cholesterol are corticosteroids, calcineurin inhibitors, and rapamycin (see page 758, 2nd column 1st full paragraph). Moore teaches that in a European multicenter study demonstrated that 44% of pateints on sirolimus had hypercholesterolemia (see page 759, 2nd column, 2nd paragraph). Moore teaches "Several lipid-lowering agents are available, but not all are appropriate for use in transplant recipients. Cholestyramine, for instance, may interfere with cyclosporin absorption, and nicotinic acid (niacin) may cause glucose intolerance, hyperuricaemia, and hepatotoxicity, as well as flushing. Fibric acid derivatives, such as gemfibrozil, have been shown to improve the LDL/HDL ratio in renal transplant patients and may have a role in recipients with hypertriglyceridaemia. However, they may not be suitable for use in liver graft recipients because of the potential to increase the incidence of gallstones" (see page 761), 2nd column, 1st paragraph).

The art teaches genetic variations and associations are often irreproducible. Hirschhorn et al. (Genetics in Medicine. Vol. 4, No. 2, pages 45-61, March 2002)

teaches that most reported associations are not robust. Of the 166 associations studied three or more times, only 6 have been consistently replicated. Hirschhorn *et al.* suggest a number of reasons for the irreproducibility of studies, suggesting population stratification, linkage disequilibrium, gene-gene or gene-environment interactions, and weak genetic effects and lack of power are possible factors that lead to such irreproducibility. Hirschhorn *et al.* caution that the current irreproducibility of most association studies should raise a cautionary alarm when considering their use as diagnostics and prognostics (p. 60, Col. 2). Thus, Hirschhorn cautions in drawing conclusions from a single report of an association between a genetic variant and disease susceptibility.

The level of skill in the art:

The level of skill in the art is deemed to be high.

Quantity of experimentation necessary:

In order to practice the invention as claimed, one of ordinary skill in the art would firs have to determine if the presence of the -31 T>C polymorphism is indicative of cholesterol status in “any” patient on “any” immunosuppressive drugs and a reliable measure to determine treatment for elevated cholesterol.

The artisan would have to undertake undue trial and error experimentation to determine if the polymorphism at -31 position of IL-1b gene is indicative of altered cholesterol in any patient. As Brenner teaches different genes and homologs have different functions in different species due to the selective pressure felt by each species, it would be unpredictable to extrapolate a finding in humans with any other species.

It would be further unpredictable to associate the -31 polymorphism with altered cholesterol levels as Wyllie teaches that the -31 has no functional effect on transcription and thus is not indicative of any disease state.

Further it would be unpredictable to associate increased cholesterol levels with the -31 mutation as the specification teaches all patients irregardless of the -31 IL-1b genotype treated with RAD had increased cholesterol levels (table 5). Thus all -31 polymorphism IL-1b genotypes appear to be predictably associated with increased cholesterol when treated with RAD. Further the specification teaches none of the patients treated with MMF had a statistical increase in cholesterol. Thus none of -31 polymorphism IL-1b genotypes appear to be predictably associated with increased cholesterol when treated with MMF. Thus the -31 polymorphism is not predictably associated with increased cholesterol due to treatment with "any" immunosuppressive drugs.

Further it would be unpredictable to associate increased cholesterol with immunosuppressive treatment based on genotype when Moore teaches that increased cholesterol is a normal effect of cholesterol levels in patients treated with immunosuppressants and the study of the specification has not been replicated, and thus is unpredictable as suggested by Hirschhorn. The specification does not provide any teachings as to the number of patients that did not have elevated cholesterol.

Further it would be unpredictable to treat any patient on immunosuppressive drugs with "any" alternative therapy as Moore teaches some alternative therapies interfere with absorption of the immunosuppressive drugs and/or have other negative

side affects. Thus Moore teaches alternative therapies are not predictable in patients treated with immunosuppressants.

The teachings of Wylie that the -511 and -31 mutations described by the instant specification have no functional transcriptional affect, it would be unpredictable to associate any mutation on the chromosome with elevated cholesterol or the response to immunosuppressive agents.

Therefor, in light of the breadth of the claims, the lack of guidance in the specification, the high level of unpredictability in the associated technology, the nature of the invention, the negative teachings in the art, and the quantity of unpredictable experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention as claimed.

10. Claims 6-10 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims broadly encompass the determining the presence of any T>C polymorphism at position -31 of “any” gene that can broadly be identified as IL-1b in “any” species. The recitation of "(position 1903 of Sequence X045000)” is not considered to be limiting as the recitation is in parenthesis. Further X04500 is not present in the sequence listing. Claim 16 is further drawn to finding "any" SNPs on "said" chromosome that are in linkage disequilibrium with the SNPs of "any" IL-1b gene

in “any” species. The claims do not set forth any structural requirements for Il-1b gene or said chromosome.

When the claims are analyzed in light of the specification, the invention encompasses an enormous number of nucleotide molecules. The specification teaches the IL-1B gene is set forth in GenBank accession X04500. The contents of GenBank accession numbers can change with sequences being added and deleted which can alter the numbering of nucleotides. Furthermore, reliance upon a SNP identification number which is referenced by a GenBank accession record does not provide adequate clarity for the claimed invention, as the content and numbering in a GenBank record can change over time as the records can be updated as time passes. In this case a potential update to the cited GenBank record wherein a revision includes the addition or deletion would result in a complete change in the numbering system. The reliance of nomenclature of SNP number scheme, which is defined by an external GenBank sequence for a numbering scheme is similar to a recitation of a trademark as the GenBank accession number record does not represent a fixed disclosure of a sequence but instead refers to a record that is constantly able to be updated and modified. In the instant application, only the nucleic acid sequences of the disclosed SEQ ID No. are described. The claims thus broadly encompass any nucleic acid sequence that can broadly be identified as IL-1b and a SNP at position -31from "any” species. Further the claim 16 is drawn to any chromosome that can broadly be identified as having a sequence that can be identified as IL-1b. This is an enormous genus of nucleic acids.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been by full structure. The instant specification teaches SEQ ID NO 3 and SEQ ID NO 4 for use in detection of the SNP at -31 in human IL-1b gene. The specification does not provide the sequence of the IL-1b or the chromosome claimed from “any” non-human species.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. other nucleotide sequences or positions with in a specific gene or nucleic acid), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case the specification provides the no structural limitation for the claimed IL-1b gene or the claimed chromosome. The claims read in light of the specification encompass any nucleic acid molecule that can broadly be identified as IL-1b with a -31 position in any species or any chromosome in any species that can broadly be identified as comprising IL-1b. This is an enormous genus of nucleic acids as Genecard (GC02M113303, 4/18/08, pages 1-15) teaches there are 440 known cDNA of Il-1b and orthlogs in at least 5 other species. Thus as the specification does not teach a single species of IL-1b or chromosome containing IL-1b, but merely 2 primers that flank a single mutation in the human Il-1b gene, the specification does not provide adequate written description.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the

'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids and polymorphisms regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The current situation is a definition of the compound solely based on its functional utility, as a polymorphism, without any definition of the particular polymorphisms claimed.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

In the instant application, the provided information regarding nucleic acid -31 polymorphism of Il-1b, do not constitute an adequate written description of the broad subject matter of the claims, and so one of skill in the art cannot envision the detailed chemical structure of the nucleic acids encompassed by the claimed polymorphism. Adequate written description requires more than a statement that nucleic acids with a particular quality are part of the invention and reference to a potential method for their identification. The nucleic acid sequence is required.

In conclusion, the limited information provided regarding -31 polymorphism of Il-1b is not deemed sufficient to reasonably convey to one skilled in the art nucleic acid molecules claimed.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 6-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-10 are indefinite over the recitation of "(position 1903 of sequence X04500)" because it is not clear if the phrase in parenthesis is a limitation of the claim and if the phrase in parenthesis is a limitation as to what is encompassed by this

phrase. The sequences and accompany text provided for each GenBank Accession No. are continuously updated and modified. Therefore, there is no single, fixed definition for the sequence presented as GenBank Accession No. X04500.

13. Claim 16 recites the limitation "said chromosome" in the third line. The claim does not previously recite “chromosome.” There is insufficient antecedent basis for this limitation in the claim. This rejection can easily be overcome by amending the claim to recite, “a chromosome.”

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by El Omar (Nature (2000) volume 404, pages 398-402).

The claim is a method of determining the identity of a nucleotide pair or haplotype which are in linkage disequilibrium with a polymorphism at -31 of the IL-1b gene. The claim depends from a claim withdrawn due to the election and thus is being interpreted as just requiring the steps of the instant claim. It is noted that amendment of the claim to depend from claim 6, will cause the withdraw of this rejection.

El Omar teaches, “Linkage disequilibrium between IL-1B231 and IL-1B2511 was almost total, with 99.5% of the inferred haplotypes (IL-1B231=IL-1B2511) in the

combined control groups consisting of either T±T or C±C (Table 1)" (see page 400, 1st column).

El Omar thus teaches a method of determining a haplotype that is in equilibrium with the -31 polymorphism of Il-1b.

Summary

No claims are allowed.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

/Sarae Bausch/
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